Cox-maze IV cryoablation and postoperative heart failure in mitral valve surgery patients

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Journal Article

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Running head: AF ablation and postoperative heart failure

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Abstract

Objective: The indications for risks and benefits of concomitant surgical ablation for atrial fibrillation (AF) have not been fully delineated. Our aim was to survey whether the Cox-maze IV procedure is associated with postoperative heart failure (PHF) or other adverse short-term outcomes after mitral valve surgery (MVS).

Design: Consecutive patients with AF undergoing MVS with (n=50) or without (n=66) concomitant Cox-maze IV cryoablation were analysed regarding perioperative data and one year mortality.

Results: The patients in the Maze group were younger, were in lower NYHA classes, had better right ventricular function, and had lower pulmonary artery pressure. The Maze group had 30 minutes longer median cross-clamp time (CCT) and 50% had PHF compared with 33% in the No-maze group, p=0.09. Two patients in the No-maze group died within one year of surgery. Congestive heart failure (OR 4.3 [CI 95%: 1.8-10], p<0.0001) and CCT (OR 1.03 [CI 95%: 1.01-1.04], p=0.001) were associated with PHF.

Conclusion: The current data cannot exclude that concomitant cryoablation increases the risk for postoperative heart failure, possibly by increasing the cross clamp time.

Introduction

Atrial fibrillation (AF) is the most common cardiac arrhythmia, with an incidence of 0.5-1% in the general population, and the prevalence increases with age (1). AF is associated with increased morbidity and mortality (1). There are several treatments for AF but the Cox-maze III cut and sew surgical procedure is the one with the best results in terms of restored sinus rhythm at long-term follow-up (2, 3). This procedure is still the reference standard for surgical treatment of AF but it is mostly used in stand-alone surgery for AF due to its technical complexity (4). Ablative lesions created with different energy sources (Cox-maze IV) have mainly replaced the cut and sew lines in AF treatment concomitant to other cardiac surgery (5, 6).

The 2012 Heart Rhythm Society/European Heart Rhythm Society/European Cardiac Arrhythmia Society guidelines recommend AF intervention as an acceptable treatment in symptomatic patients, concomitant to other cardiac surgery (7). Theories and studies that suggest a decreased risk for stroke, an improved quality of life, a decreased risk for heart failure, and an improved survival with achievement of sinus rhythm after cardiac surgery have led to a more liberal implementation of concomitant AF procedure, particularly in mitral valve surgery (MVS) (7, 8).

AF treatment added to other cardiac surgery does not seem to increase short-term mortality, reoperation for bleeding, stroke, low cardiac output syndrome, deep sternal wound infection, prolonged ventilation, or renal failure (8-10). However, it increases the cross-clamp time (CCT) and the intensive care unit stay, and it may increase the need for a permanent pacemaker postoperatively (8, 11-13).

Postoperative heart failure (PHF) is one of the major determinants for adverse outcome in cardiac surgery (14-16). Most of the in-hospital mortality after coronary bypass surgery is

related to PHF, and patients with PHF after surgery for aortic stenosis have a 42% mortality rate at five-year follow-up (16). Our hypothesis was that the Cox-maze IV cryoablation procedure added to MVS is associated with PHF and other adverse short-term outcomes.

Material and methods

Consecutive patients with preoperative nonparoxysmal AF undergoing MVS between Nov 2009 and June 2013 were identified in our institutional database. Sixty-six patients had no concomitant ablation procedure (No-maze group) and 50 patients had concomitant Cox-maze IV biatrial cryoablation (Maze group), using the argon powered Cardioblate® CryoFlex™ Surgical Ablation Probe (Medtronic Inc., Minneapolis, MN, USA). The decision to add the Cox-maze IV procedure to MVS was made by the surgeon. The cryoablation probe was applied for 120 seconds at full power and usually it reached -150°C but always at least -130°C. The removal of the probe was aided by irrigation with warm saline. The left atrial lesion set consisted of a circular line isolating the four pulmonary vein orifices, a coronary sinus lesion from the atrial incision through the mitral annulus, and a left atrial appendage line connected to the circular pulmonary vein lesion. The right atrial lesions included an intercaval line between the superior and the inferior vena cava crossing the right atrial incision, a “T” lesion from the right atrial incision to the posterior portion of the tricuspid annulus, and a lesion from the right atrial appendage to the anterior portion of the tricuspid annulus (17).

Mitral valve repair was performed in 34(68%) of the patients in the Maze group and in 46(70%) of the patients in the No-maze group. The left atrial appendage was suture-closed from the inside of the left atrium in 10(20%) of the Maze patients and in 4(6%) of the No-maze patients, p=0.04.

The procedures were performed by nine consultant surgeons and three of them performed 99 of the 116 operations. The perioperative care was supervised by 14 consultant anaesthesiologists. Clinical data and mortality were collected retrospectively from the institutional database, clinical records, and from the Swedish Civil Registry. One-year rhythm outcome was based on multiple electrocardiograms, on 24 – 48 hours Holter monitoring (33%), and on registrations from permanent pacemakers (29%) in the period from 10 to 14 months postoperatively. Study approval was obtained from the Regional Ethical Review Board in Linköping, Sweden (Dnr. 2012/371-31).

PHF was defined as a haemodynamic state when the cardiac output does not meet the systemic demand without supportive measures other than correction of volume or vascular resistance. Such supportive measures or treatment consisted of an intra-aortic balloon pump or ventricular assist device, or infusion of one or more inotropes for more than 30 minutes in dosages as listed below: Epinephrine ≥0.033 mg/kg of body weight per minute, milrinone ≥0.375 mg/kg of body weight per minute, dopamine ≥4 mg/kg of body weight per minute, dobutamine ≥4 mg/kg of body weight per minute, or levosimendan regardless of dose.

Clinical management

Standard monitoring was used consisting of a five-lead electrocardiogram, pulse oximetry, continuous arterial blood pressure monitoring, central venous pressure, and transoesophageal echocardiography. A median sternotomy was performed and combined anterograde and retrograde blood cardioplegia was employed in all patients. A surgical pulmonary artery catheter was introduced in all patients before weaning from extracorporeal circulation (18).

Echocardiography

Images were recorded from standard views, according to the recommendations of the American Society of Echocardiography for transthoracic studies (19). The long-axis parasternal view was used to derive the M-mode measurement of the left ventricular diameter. The right ventricular inflow diameter and the left and right atrial areas were calculated from the four chamber view. Tricuspid annular plane systolic excursion was recorded at the right ventricular free wall using the cross sectional guided M-mode. The systolic pulmonary arterial pressure was calculated using the tricuspid regurgitation velocity to obtain a systolic trans-valvular pressure gradient. Estimated right atrial pressure based on vena cava size and collapse was then added to the obtained gradient. The systolic left ventricular function was assessed using eyeballing combining the regional ventricular function abnormalities and the haemodynamic adaptation to eventual volume overload. The result was graded in normal, mild, moderate or severe left ventricular dysfunction.

Statistical analysis

Categorical variables are presented as numbers (percent) and continuous variables as medians (1^{st} – 3^{rd} quartile). Nonparametric tests (Mann-Whitney U test and Fisher's exact test) were used for comparison between groups. Kaplan-Meier analysis was conducted to illustrate the cumulative survival for the groups. Univariate logistic regression was used for the evaluation of the association between different variables and PHF. Collinearity diagnostics were performed and no signs of multicollinearity were found. The confounding effects of congestive heart failure, CCT, and cryo-maze ablation were tested in a multivariate model. None of the two other variables changed the odds ratio of CCT for PHF > 10%. Statistical analyses were performed with computerized statistical packages (Statistica 10.0, StatSoft Inc, Tulsa, OK, USA) and IBM SPSS Statistics 22.0 (IBM Corp., Armonk, NY, USA.).

Results

The surgical procedures are listed in Table 1. Fewer coronary artery bypass procedures were performed in the Maze group compared to the No-maze group, five(10%) v 21(32%), p=0.006.

Preoperative and intraoperative data

The baseline characteristics for both groups are given in Table 2. The patients in the Maze group were younger, less frequently had a history of angina pectoris, were in lower NYHA classes, had higher blood haemoglobin, and they also had higher creatinine clearance. On the echocardiogram, tricuspid annular plane systolic excursion was higher and the pulmonary artery pressure was lower in the Maze group. However, there was no significant difference in EuroSCORE II between the groups. CCT was 127(111-140) and 97(79-118) minutes ($p<0.0001$), extracorporeal circulation time was 178(154-209) and 140(109-169) minutes ($p<0.0001$), and surgery time was 257(223-315) and 220(190-280) minutes ($p=0.001$) in the Maze group and in the No-maze group, respectively.

Postoperative outcomes

Markers for myocardial injury were significantly higher in the Maze group on the first postoperative day. Postoperative in-hospital results are shown in Table 3. At discharge from our hospital, 32(64%) of the patients in the Maze group were free from AF and at the one-year follow-up, 40(83%) had no evidence of AF. The need for permanent pacemaker

implantation was 11(22%) v 14(21%), p=0.82, at one month and 13(26%) v 16(24%), p=1.0 at the one-year follow-up in the Maze group and in the No-maze group, respectively. The Kaplan-Meier cumulative proportional survival curves are shown in Figure 1.

Postoperative heart failure

PHF presented in all patients at weaning from extracorporeal circulation except for two patients in each group in whom PHF was evident within 24 hours after surgery. Eight patients (16%) in the Maze group and 20 patients (30%) in the No-maze group (p=0.8) were weaned from extracorporeal circulation without any inotrope support. Two patients needed an intra-aortic balloon pump in the Maze group at weaning from cardiopulmonary bypass. They had CCT of 144 and 240 minutes and the intra-aortic balloon pump treatments lasted for one and four days, respectively. One patient in each group was treated with an extracorporeal membrane oxygenator. The patient in the Maze group had CCT for 172 minutes and the extracorporeal membrane oxygenation treatment started at weaning from extracorporeal circulation and lasted for nine days. The patient in the No-maze group had CCT for 105 minutes and a postoperative coagulopathy leading to four reoperations for bleeding within 24 hours from the index surgery. The extracorporeal membrane oxygenation treatment started after the fourth reoperation and lasted for six days.

Patients with PHF (n=47) needed longer ventilator treatment (7 [7-18] v 4 [3-5] hours, p<0.0001), a longer time in the intensive care unit (28 [21-91] v 21 [20-22] hours, p=0.0002), and more of the PHF patients had >50% postoperative creatinine elevation (15% v 4%, p=0.04) compared with the patients without PHF (n=69). One patient with PHF and one without PHF died within the one-year follow-up period.

Variables associated with PHF

Univariate associations between PHF and variables of interest are given in Table 4. No confounding effects were found between congestive heart failure, CCT, and cryo-maze ablation in relation to PHF. In the multivariate model CCT had OR 1.02 [CI 95%: 1.01-1.04] (p=0.008) and congestive heart failure had OR 3.5 [CI 95%: 1.5-8.4], p=0.005 in association with PHF. Cryo-maze ablation did not reach statistical significance when it was included in the model (OR 1.1 [CI 95%: 0.5-2.9], p=0.8) and it did not significantly influence the impact of CCT and congestive heart failure. An exclusion of CCT from the model did not make cryo-maze ablation become significantly associated with PHF (OR 1.9 [CI 95%: 0.9-4.3], p=0.11).

Discussion

Surgeons' concern about increased morbidity associated with the Cox-maze IV procedure may partly explain why most of the cardiac surgery patients with AF are left untreated in spite of the present recommendations (8, 20, 21). The selection of patients for concomitant surgical AF treatment is based on symptoms but is also influenced by expected success contra complication rates. In the case of structural cardiac pathology, arrhythmia-related symptoms such as fatigue and effort intolerance are often difficult to distinguish from symptoms related to valve dysfunction. As seen in our study, MVS in patients with AF includes, to a large extent, patients in need of other cardiac surgery procedures, which increases the surgical complexity and suggests a higher risk of adverse outcomes. Better definition of parameters correlated to adverse outcome would enhance patient selection.

The connection we found between PHF and early postoperative morbidity is in accordance with previous studies on other patient categories (14, 16, 22). The incidence of PHF was 41% in patients with AF undergoing MVS in our study, which is higher than the reported 5-15% of

PHF for other cardiac surgery patient groups (23-26). In this study, PHF presented at weaning from extracorporeal circulation and was associated with prolonged respiratory treatment and increased renal impairment. The 2.0% one-year mortality in patients with PHF was lower than the predicted early postoperative mortality indicated by EuroSCORE II (5.8%) and it was considerably lower than in patients with PHF after coronary surgery (25.5%) (16). In patients with PHF after surgery for aortic stenosis, an 8.9% one-year mortality was reported but the mortality rose to 42.2% at the five-year follow-up (16). Obviously the impact of PHF on postoperative mortality is different for different patient groups. Whether PHF has a larger impact on the long-term mortality than it has on the one-year mortality in patients with AF undergoing MVS remains to be shown.

Patients in the Maze group were younger, had a lower rate of coronary artery disease, were in lower NYHA classes, had a higher blood haemoglobin level, higher creatinine clearance, better longitudinal right ventricle function, and lower pulmonary artery pressure. However, we found no significant differences in postoperative outcome with regard to mortality, stroke, reoperation for bleeding, postoperative renal failure or length of intensive care unit stay between the two groups.

In spite of the more favourable preoperative state of the Maze group, the incidence of PHF was close to significantly higher compared with the No-maze group (50% v 33%, p=0.09). The strong association of CCT and congestive heart failure with PHF was, however, not confounded by the Cox-maze IV procedure. We cannot preclude that the Cryo-maze procedure increases the risk of PHF in patients with congestive heart failure undergoing complex cardiac surgery, not least by adding approximately 30 minutes to the CCT.

Preoperative left ventricular dysfunction seems to play a less important role for PHF after MVS in patients with AF than in patients operated upon for aortic stenosis (22). Perioperative myocardial infarction is related to PHF after both coronary and aortic stenosis surgery (22,

23). The cryoablation procedure itself results in elevation of markers for myocardial injury by atrial myocyte destruction (27). This prevents evaluation of the perioperative ventricular injury and thereby the diagnosis of perioperative myocardial infarction.

The Cox-maze IV cryoablation procedure seems not to affect the need for a permanent pacemaker when conducted concomitant to MVS in spite of the 83% freedom from AF in the Maze group at the one-year follow-up. The reported freedom of AF one year after MVS without concomitant AF procedure is varying from approximately 30-43% (12,28).

This study has certain limitations that should be acknowledged. It was not prospective and the patient selection for concomitant maze surgery was based on the surgeon's decision which means the groups were not fully comparable. Conclusions on outcome comparisons between the groups must be made with caution. The limited size of the groups and the low incidence of early postoperative mortality impede an analysis of factors related to one-year mortality. There is no generally accepted criterion for PHF and our definition is dependent on the individual judgement of various surgeons and anaesthesiologists which may partly explain the high incidence of PHF in our patients with AF undergoing MVS. However, this definition of PHF applied on aortic valve surgery and coronary artery surgery resulted in 11% and 12% of PHF, respectively, which is comparable whith the 5-15% of PHF in other studies on aortic valve and coronary artery surgery (23). At our institution a reliance on mixed venous oxygen saturation and echocardiographic appearance rather than fixed haemodynamic criteria are used to diagnose PHF (22, 23).

Summary

We cannot exclude that the addition of the Cox-maze IV cryoablation procedure to MVS increases the risk for postoperative heart failure. It can, however, be conducted with a low

one-year mortality at least in a selected group of younger patients in a lower New York Heart Association class, and with a better renal function. A concomitant cryo-maze procedure should be applied with caution in patients needing complex surgical procedures with long expected CCT. PHF after MVS in patients with preoperative AF is frequent and results in prolonged ventilator treatment and increased time in the intensive care unit.

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Tables

Table 1. The different surgical procedures performed.

	Maze n=50	No-maze n=66
MVS	7	11
MVS + TVS	35	30
MVS + CABG	1	9
MVS + AVR	1	2
MVS + aortic surgery	0	1
MVS + TVS + CABG	3	10
MVS + TVS + AVR	2	1
MVS + TVS + AVR + CABG	1	1
MVS + TVS + CABG + AVR + aortic surgery	0	1

AVR = aortic valve surgery; CABG = coronary artery bypass grafting; MVS = mitral valve surgery; TVS = tricuspid valve surgery.

Table 2. Baseline patient characteristics.

	Maze n=50	No-maze n=66	*p* Value
Age (years)	68 (64-74)	75 (67-78)	0.001
Female gender	16 (32%)	23 (35%)	0.84
Body mass index (kg/m^2)	25 (23-27)	26 (23-28)	0.42
Insulin or orally treated diabetes mellitus	0	2 (3%)	0.23
Chronic obstructive pulmonary disease	2 (4%)	4 (6%)	0.70
Cerebrovascular disease	5 (10%)	6 (9.2%)	1.0
Peripheral artery disease	3 (6%)	4 (6.1%)	1.0
Hypertension	14 (57%)	29 (44%)	0.12
Angina pectoris	2 (4%)	18 (27%)	0.001
History of congestive heart failure	32 (64%)	37 (56%)	0.45
New York Heart Association class III/IV	26 (52%)	57 (86%)	0.0001
EuroSCORE II	3.7 (2.3-6.3)	4.1 (2.6-6.3)	0.50
Blood Haemoglobin (g/L)	143 (133-152)	134 (124-144)	0.002
Creatinine clearance (ml/min)	75 (61-89)	63 (46-86)	0.03
Creatinine clearance <50 ml/min	9 (18%)	21 (32%)	0.13
Previous cardiac surgery	1 (2%)	5 (8%)	0.23
Previous myocardial infarction within 90 days	1 (2%)	5 (8%)	0.24
Echocardiography data			
LV dysfunction moderate or severe	4 (8%)	10 (16%)	0.26
LV diameter index (LV/BSA(mm/m^2))	29 (26-31)	30 (27-33)	0.13
RV diameter index (RV/BSA(mm/m^2))	21 (19-23)	21 (19-23)	0.97
LA area index (LA/BSA(mm^2/m^2))	17 (14-20)	17 (14-20)	0.57

RA area index (RA/BSA(mm^2/m^2))	12 (10-14)	13 (11-15)	0.13
Tricuspid annular plane systolic excursion (mm)	19 (17-22)	17 (15-20)	0.008
Pulmonary artery pressure (mmHg)	40 (35-45)	45 (40-55)	0.001

Results are given as n (%) or as median (1^{st} – 3^{rd} quartile). BSA = body surface area; LA = left atrium; LV = left ventricle; RA= right atrium; RV = right ventricle.

Table 3. Postoperative in-hospital outcomes.

	Maze n=50	No-maze n=66	*p* Value
Plasma ASAT, day 1 (µkat/L)	3.7 (3.0-4.5)	1.4 (1.1-2.0)	<0.0001
Plasma CK-MB, day 1 (µg/L)	118 (94-147)	33 (26-50)	<0.0001
Plasma Creatinine elevation >50%	4 (8%)	6 (9%)	1.0
Plasma Creatinine at discharge (µmol/L)	77 (60-92)	84 (72-102)	0.03
Dialysis	1 (2%)	2 (3%)	1.0
Time on ventilator (h)	5 (3-9)	4 (3-8)	0.18
Time on ventilator >24 hrs	7 (14%)	4 (6%)	0.20
ICU-stay (h)	57 (44-103)	46 (43-96)	0.19
ICU-stay >72 hrs	8 (16%)	12 (18%)	0.81
Reoperation for tamponade/bleeding	3 (6%)	3 (3%)	0.70
Reoperation for sternal infection	1 (2%)	1 (2%)	0.43
Stroke	0	0	
Postoperative heart failure	25 (50%)	22 (33%)	0.09

Results are given as n (%) or as median (1^{st} – 3^{rd} quartile). ASAT = Aspartate aminotransferase; CK-MB = Creatine kinase-muscle, brain isotype; ICU = Intensive care unit.

Table 4. Univariate analysis of potential risk factors for PHF.

Variable	n (%) of patients	PHF n (%)	Odds Ratio	CI(95%)	*p* Value
Patients	116	47 (41%)			
Sex					
Male	77 (66%)	35 (45%)	1.00		
Female	39 (34%)	12 (31%)	0.53	0.2-1.2	0.13
Age (years)					
<70	53 (46%)	24 (45%)	1.00		
70-79	49 (42%)	20 (41%)	0.8	0.4-1.8	0.65
≥80	14 (12%)	3 (21%)	0.33	0.1-1.3	0.11
Mean: 70			0.96	0.9-1.01	0.11
Congestive heart failure					
No	47 (38%)	10 (21%)	1.00		
Yes	69 (59%)	37 (54%)	4.28	1.8-10	<0.0001
Peripheral artery disease					
No	108 (94%)	43 (40%)	1.00		
Yes	7 (6%)	4 (57%)	2.01	0.4-9.6	0.04
Creatinine clearance <50 mL/minute					
No	86 (74%)	31 (36%)	1.00		
Yes	30 (26%)	16 (53%)	2.03	0.9-4.7	0.01
Mean: 70			0.99	0.98-1.01	0.28
New York Heart Association class					
I/II	33 (28%)	10 (30%)	1.00		

III/IV	83 (72%)	37 (45%)	1.85	0.8- 4.4	0.16
RV diameter index (RV/BSA(mm/m^2))					
Mean: 21			1.09	0.96-1.2	0.17
LV ejection fraction ≥40%					
Yes	100 (88%)	38 (38%)	1.00		
No	14 (12%)	8 (57%)	2.17	0.7-6.8	0.2
TAPSE <20mm					
No	70 (65%)	32 (46%)	1.00		
Yes	38 (35%)	11 (29%)	2.07	0.9-4.9	0.09
Mean: 18			0.91	0.8-1.02	0.1
Cryoablation					
No	66 (57%)	22 (33%)	1.00		
Yes	50 (43%)	25 (50%)	2.00	0.9-4.3	0.07
Cross-clamp time (minutes)					
<120	70 (60%)	19 (27%)	1.00		
120-150	37 (32%)	21 (57%)	3.50	1.5-8.2	0.003
>150	9 (8%)	7 (78%)	9.40	1.7- 50	0.008
Mean: 112			1.02	1.01-1.04	0.001

AF = atrial fibrillation; BSA = body surface area; CI = confidence interval; LV = left ventricle; PHF = postoperative heart failure; RV = right ventricle; TAPSE = tricuspid annular plane systolic excursion.

Table legends

Table 1. AVR = aortic valve surgery; CABG = coronary artery bypass grafting; MVS = mitral valve surgery; TVS = tricuspid valve surgery.

Table 2. Results are given as n (%) or as median (1st – 3rd quartile). BSA = body surface area; LA = left atrium; LV = left ventricle; RA= right atrium; RV = right ventricle.

Table 3. Results are given as n (%) or as median (1^{st} – 3^{rd} quartile). ASAT = Aspartate aminotransferase; CK-MB = Creatine kinase-muscle, brain isotype; ICU = Intensive care unit.

Table 4. AF = atrial fibrillation; BSA = body surface area; CI = confidence interval; LV = left ventricle; PHF = postoperative heart failure; RV = right ventricle; TAPSE = tricuspid annular plane systolic excursion.

Figure legend

Figure 1. Kaplan-Meier cumulative proportion survival curves for patients with and without concomitant Cox-maze IV cryoablation procedure.

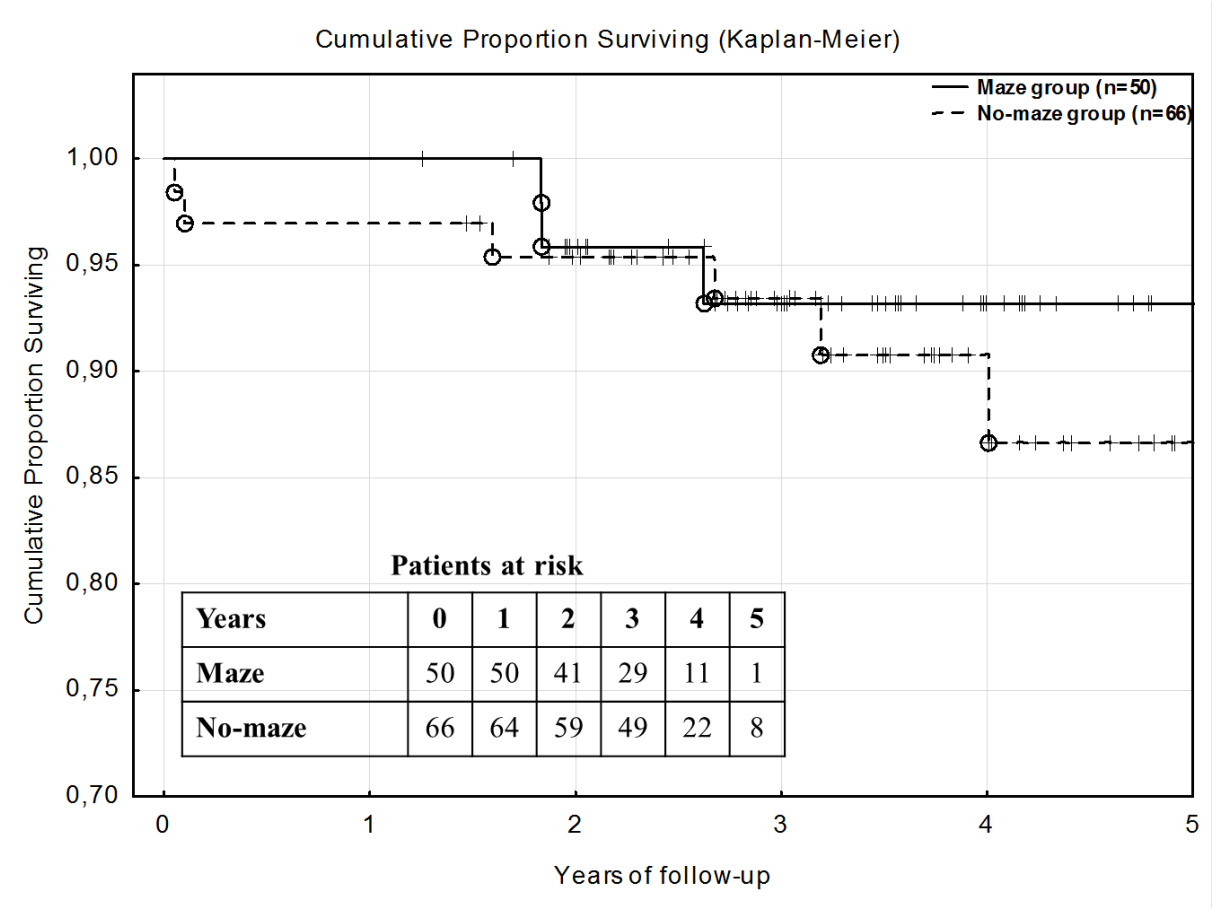

Figure 1. Kaplan-Meier cumulative proportion survival curves for patients with and without concomitant Cox-maze IV cryoablation procedure.